REMARKS

The foregoing amendments and the following remarks are submitted in response to the communication dated January 15, 2004.

The Examiner has objected to the specification because on page 25, line 11, "JAC" should be "JAK". Applicants have amended the specification to correct this. The Examiner as further objected to the title of the Application as not descriptive and requires a new title. The Examiner suggests the title "DB, the Receptor for Leptin". Applicants have above amended the title as requested by the Examiner.

Status of the Claims

Claims 3-5, 7-9, 63, 66 and 68 are pending in the application. Claims 6, 14-62, 64, 65 and 67, which are withdrawn from consideration, have been canceled without prejudice. Claims 3, 4, 5, 7, 8, 66 and 68 have been amended in order to more particularly point out and distinctly claim that which Applicants regard as the invention. Support for the amended claims can be found generally through Applicants' specification.

Oath/Declaration

The Examiner has objected to the oath or declaration as defective, asserting that only one Declaration and Power of Attorney form is present in the case. The Examiner remarks that the signatures of the two inventors other than Ricardo Proenca are missing. Applicants respectfully disagree and assert that on July 22, 1996 a Submission of Missing Parts in Application was filed with the U.S. PTO, including two (2) combined Declaration and Power of Attorney forms, one executed by Ricardo Proenca, and a second executed by both Jeffrey M. Friedman and Gwo-Hwa Lee. Applicants submit a copy of the postcard, Notice submission and the Declaration and Power of Attorney form executed by inventors Friedman and Lee. Applicants respectfully request that such Declaration and Power of Attorney form, properly executed by the inventors Friedman and Lee on July 22, 1996 and June 5, 1996 respectfully, and previously timely submitted by Applicants, be placed with and entered in the file wrapper to properly provide an oath or declaration for this Application.

Claim Objections

The Examiner objects to claims 3-5, 7-9 and 68 as they encompass non-elected inventions and requests appropriate correction. Applicants have above amended the claims to delete the non-elected inventions, without prejudice.

The Examiner objects to claim 7 because it is not in sequence compliance. Applicants have above amended claim 7 to refer particularly to the hybrid truncated receptor polypeptide of amino acids 28-805 of SEQ ID NO: 10, as suggested by the Examiner. Applicants have further above amended the specification to appropriately and consistently identify this hybrid receptor polypeptide. As stated by the Examiner at page 5 of the January 15, 2004 Office Action, Applicants assert and point out that this amendment does not constitute new matter.

The Examiner has rejected claim 68 as being indefinite because it is an improper dependent claim, referring to a "leptin receptor of any of claims 3-9". Applicants have above amended claim 68 to refer to the leptin receptor of any one of claims 3-5 or 7-9, as suggested by the Examiner.

In view of the foregoing amendments and remarks, Applicants submit that the Examiner's claim objections are obviated and should be withdrawn.

The 35 USC § 101 Rejection

Claims 3-5, 7-9 and 68 have been rejected under 35 U.S.C. 101 as directed to non-statutory subject matter. Applicants have above amended independent claims 3, 5, 7 and 8 to refer particularly to "isolated" and assert that this rejection should now be properly withdrawn.

The Specification Fully Enables the Claimed Invention

The Examiner has rejected claim 66 under 35 U.S.C. 112, first paragraph, because the Examiner asserts that the specification does not enable any person skilled in the art to which it pertains, or with which it is most connected, to make and use the invention commensurate in scope with these claims. The Examiner asserts that Claim 66 is not enabled for a composition comprising a soluble leptin receptor that would result in weight loss. Applicants respectfully

disagree. Applicants have above amended claim 66 to refer to "modulating" body weight, which encompasses and includes weight gain or weight loss. The Examiner appropriately commented that a soluble receptor, which binds leptin in the circulation, could result in weight gain. In addition, a soluble receptor could also be expected to result in weight loss, particularly in that binding circulating leptin in an individual expressing a mutant leptin causing weight gain could block the weight gain.

Claims 3-5, 7, 8, 63, 66 and 68 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. The Examiner asserts that the claims as written include polypeptides comprising fragments and homologues, and encompass polypeptides that vary substantially in length and also in amino acid composition. The Examiner states that the instant disclosure does not adequately support the scope of the claimed genus, under written description, which encompasses a substantial variety of subgenera. Applicants respectfully disagree and assert that Applicants have described and provided examples of soluble leptin receptors which support a genus claim. Applicants have described and provided the specific DNA and protein sequence for soluble receptor species OB-Re (SEQ ID NO:10) as well as the truncated variant of amino acids 28-805 of SEQ ID NO: 10. This species was isolated as a naturally occurring soluble receptor species, using procedures and methods detailed in the specification. The skilled artisan could readily, and without undue experimentation, isolate additional species of the genus of such soluble receptor(s), including additional and related allelic variants thereof.

In view of the foregoing remarks, Applicants submit that the Examiner's rejections under 35 U.S.C. 112, first paragraph may properly be withdrawn.

The 35 USC § 102 Rejection

Claims 8, 63, 66 and 68 are rejected under 35 U.S.C. 102(e) as being anticipated by Tartaglia et al U.S. Patent No. 6,506,877, filed December 28, 1995. In particular, the Examiner states that Tartaglia et al. discloses a protein (SEQ ID NO: 2) that is 100% identical to amino

acids 1-796 of SEQ ID NO: 10 of the instant invention. Applicants submit that Tartaglia et al. does not anticipate the soluble leptin receptor of the instant invention and claimed by Applicants. Anticipation is a question of fact. As defined by the Federal Circuit, "[t]o anticipate a claim a reference must disclose every element of the challenged claim and enable one skilled in the art to make the anticipating subject-matter." *PPG Industries, Inc. vs Guardian Industries Corp., 37 USPQ2d 1618 (Fed. Cir. 1996) (emphasis added).* Tartaglia et al neither discloses every element of the rejected claims nor enables one skilled in the art to make the anticipating subject matter, specifically the soluble receptor of SEQ ID NO: 10 or the hybrid variant of SEQ ID NO: 10. SEQ ID NO: 2 of Tartaglia does not correspond to a soluble receptor, nor does it correspond in sequence to the soluble receptor(s) of the instant Application. As detailed in Tartaglia et al at page 6, lines 52-57, the deduced amino acid sequence (SEQ ID NO:2) of murine ObR protein has domains as follows:

> signal sequence (amino acid residues 1 to about 22), extracellular domain (from about amino acid residue 23 to about 837), transmembrane domain (from about amino acid residue 838 to about 860), and cytoplasmic domain (from about amino acid residue 861 to 894.

SEQ ID NO: 2 of Tartaglia thus is not a soluble receptor and in fact includes a transmembrane and cytoplasmic domain. Applicants further point out that, as described in the instant specification, including at page 86, lines 28-30, soluble receptor OB-Re (SEQ ID NO:10) predicts a different amino acid sequence after His^{796}. The Tartaglia sequence of SEQ ID NO:2 corresponds to SEQ ID NO: 10 up until His^{796}, as indicated by Applicants, but does not teach or anticipate the unique C-terminal sequence of SEQ ID NO:10. Further, this C-terminal sequence after His^{796} in Ob-Re is not even suggested by Tartaglia. In addition, Tartaglia describes an extracellular domain from about amino acid residue 837 and does not teach or anticipate, or even suggest, the end of natural DB sequence at amino acid His^{796} in a soluble receptor form. Tartaglia et al. does not teach or anticipate the soluble receptor(s) as claimed by Applicants.

In view of the foregoing remarks, Applicants submit that the Examiner's rejection under 35 U.S.C. 102 may properly be withdrawn.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks in the file history of the instant Application. The Claims as amended are believed to be in condition for allowance, and reconsideration and withdrawal of all of the outstanding rejections is therefore believed in order. Early and favorable action on the claims is earnestly solicited.

Respectfully submitted,
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Complete Listing of Claims in Application U.S.S.N. 08/586,594

Claims 1-2 (cancelled)

Claim 3 (presently amended) An isolated leptin receptor (OB-R) polypeptide which is a soluble receptor and which is encoded by a nucleic acid which is identifiable with a polymerase chain reaction (PCR) probe selected from group consisting of a probe for clone 7 (forward primer SEQ ID NO:42 and reverse primer SEQ ID NO:43), a probe for clone 11 (forward primer SEQ ID NO:44 and reverse primer SEQ ID NO:45), and both clone 7 and clone 11.

Claim 4 (presently amended) The leptin receptor of claim 3, which is encoded by a nucleic acid which is identifiable with a PCR probe selected from the group consisting of ~~a probe for clone 42 (forward primer SEQ ID NO:26 and reverse primer SEQ ID NO:46); a probe for clone 46 (forward primer SEQ ID NO:47 and reverse primer SEQ ID NO:48); a probe for clone 58 (forward primer SEQ ID NO:47 and reverse primer SEQ ID NO:50);~~ a probe for clone S14 (forward primer SEQ ID NO:51 and reverse primer SEQ ID NO:52); and a probe for clone S3 (forward primer SEQ ID NO:53 and reverse primer SEQ ID NO:54).

Claim 5 (presently amended) An isolated leptin receptor (OB-R) polypeptide which is ~~selected from the group consisting of OB-Ra (SEQ ID NO:2), OB-Rb (SEQ ID NO:4), OB-Rc (SEQ ID NO:6), OB-Rd (SEQ ID NO:8), and~~ OB-Re (SEQ ID NO:10), or allelic variants thereof.

Claim 6 (cancelled)

Claim 7 (presently amended) An isolated leptin receptor (OB-R) polypeptide of amino acids 28-805 of SEQ ID NO: 10, or allelic variants thereof. ~~wherein~~

~~a) the N-terminal sequence is selected from the group consisting of~~

~~i. amino acid residues 1-889 (SEQ ID NO:80);~~

~~ii. amino acid residues 23-889 (SEQ ID NO:81);~~

~~iii. amino acid residues 28-889 (SEQ ID NO:82);~~

~~iv. amino acid residues 133-889 (SEQ ID NO:83);~~

~~v. amino acid residues 733-889 (SEQ ID NO:84);~~

~~vi. amino acid residues 1-796 (SEQ ID NO:85);~~

~~vii. amino acid residues 23-796 (SEQ ID NO:86);~~

~~viii. amino acid residues 28-796 (SEQ ID NO:87);~~

ix. ~~amino acid residues 133-796 (SEQ ID NO:88);~~

~~x. amino acid residues 733-796 (SEQ ID NO:89); and~~

~~xi) allelic variants of any of subparts i) through x); and~~

~~b) the C-terminal sequence is selected from the group consisting of~~

~~i) SEQ ID NO:11;~~

~~ii) SEQ ID NO:12;~~

~~iii) SEQ ID NO:13;~~

~~iv) SEQ ID NO:14;~~

~~v) SEQ ID NO:15 after His^{796} (SEQ ID NO:90); and~~

~~vi) allelic variants of any of subparts i) through v);~~

~~wherein the numbering in subpart a) is based on the amino acid sequence of SEQ ID NO:55.~~

Claim 8 (presently amended) An isolated leptin receptor (OB-R) polypeptide which is a soluble receptor.

Claim 9 (previously amended) The soluble leptin receptor of Claim 8 which is selected from the group consisting of

a) OB-Re (SEQ ID NO:10);

b) an N-terminal sequence which is selected from the group consisting of:

i) OB-Ra (SEQ ID NO:2),

ii) OB-Rb (SEQ ID NO:4),

iii) OB-Rd (SEQ ID NO:8), and

iv) corresponding to SEQ ID NO:55 from Pro^{664}, through His^{796} [His^{799}], and a C-terminal sequence which is OB-Re from His^{796} (SEQ ID NO:91); and

v) allelic variants of any of subparts i) through iv);

c) an N-terminal sequence which is selected from the group consisting of

i) amino acid residues 1-796 (SEQ ID NO:85);

ii) amino acid residues 23-796 (SEQ ID NO:86);

iii) amino acid residues 28-796 (SEQ ID NO:87);

iv) amino acid residues 133-796 (SEQ ID NO:88);

v) amino acid residues 733-796 (SEQ ID NO:89); and

vi) allelic variants of any of subparts i) through v); and

a C-terminal sequence which is SEQ ID NO:15;

wherein the numbering in subparts b) and c) is based on the amino acid sequence of SEQ ID NO:55.

Claims 10-62 (cancelled)

63. A pharmaceutical composition comprising a soluble leptin receptor according to any of claims 8 or 9, and a pharmaceutically acceptable carrier.

Claims 64-65 (cancelled)

66. A body appearance improving cosmetic composition for modulating ~~reducing~~ the body weight of an individual comprising a soluble leptin receptor of claim 8 or 9, and an acceptable carrier.

Claim 67 (cancelled)

68. The leptin receptor of any one of Claims 3-7 and 7-9 ~~3-9 and 14~~ which is a murine leptin receptor